Citation:

Kojima M, Wakai K, Tamakoshi K, Tokudome S, Toyoshima H, Watanabe Y, Hayakawa N, Suzuki K, Hashimoto S, Ito Y, Tamakoshi A; Japan Collaborative Cohort Study Group. Diet and colorectal cancer mortality: Results from the Japan Collaborative Cohort Study. *Nutr Cancer.* 2004; 50 (1): 23-32

PubMed ID: 15572294

Study Design:

Prospective cohort study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the association between diet and colorectal cancer risk in Japanese adults.

Inclusion Criteria:

- Subjects participating in the Japan Collaborative Cohort Study for Evaluation of Cancer Risk
- Adults aged 40-79 years
- Enrolled between 1988-1990 in 45 areas throughout Japan.

Exclusion Criteria:

- History of colorectal cancer
- If baseline questionnaire did not include the dietary section or who skipped questions about diet.

Description of Study Protocol:

Recruitment

1988-1990.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

- Food-frequency questionnaire (FFQ) where participants were asked to categorize how often on average they consumed each of 33 foods typical in Japanese diet
- Nutrition experts working on the study validated that questionnaire in 85 subjects from 14 study areas
- Subjects recorded three-day diet records every three months for a years and then filled out the FFQ again
- Spearman correlations coefficients between the first and second FFQ for the 33 items ranged from 0.4-0.8.

Blinding Used

None.

Intervention

None.

Statistical Analysis

The risk of colon and rectal cancer were evaluated separately by sex. Data were analyzed by SAS version 8.2 (Cary, North Carolina).

- Hazard ratios (HR) and 95% CIs for colon and rectal cancer according to intake frequencies for specific food items, were estimated sing Cox's proportional hazard models through the PHREG procedure in SAS
- Intake data were re-categorized as high, middle, low consumption for each food
- Linear trends in association of food and cancer risk were calculated based on assigned values: One, zero to two times per month, one to two times per week, three to four times per week and almost every day were entered as a continuous variable in the proportional hazard mode
- Subjects were grouped according to region and the "strata" statement of the PHREG procedure was used to consider regional differences
- The models were adjusted for the following:
    - Age, time spent walking daily (≤min≥30 minutes)
    - Age at leaving full time education (>18 years or≤18 years)
    - History of colorectal cancer in parents or siblings (yes or no)
    - Body mass index (BMI) (≥ 25or≤25kg/m^2)
    - Frequency of alcohol intake (at least five days per week or
    - Current smoking status (smoker or non-smokers)
      For each covariate, missing values were treated as an additional category in the variable and were included in the model
- Two-tailed P-values of≤0.05 were considered significantly different.

Data Collection Summary:

Timing of Measurements

1998-1990.

Dependent Variables

Fatal death due to colon or rectal cancer confirmed by death certificates.

Independent Variables

Dietary intake.

Control Variables

- Age
- Time spent walking daily
- Age at leaving full-time education
- History of colorectal cancer in parents or siblings
- BMI
- Frequency of alcohol intake
- Current smoking status.

For each covariate, missing values were treated as an additional category in the variable and were included in the model.

Description of Actual Data Sample:

- *Initial N:* 110,792
- *Attrition:* 107, 824 (45,181 men and 62,643 women)
- *Age:* 40-79 years
- *Ethnicity:* Japanese
- *Other relevant demographics:* Not applicable
- *Anthropometrics:* Unclear

- *Location:* Six regions in Japan:
  - Hokkaido/Tohoku
  - Kanto
  - Tokai
  - Kinki
  - Chugoku
  - Kyushu.

Summary of Results:

- The average follow-up period was 9.9±2.2 years or 1,064,448 person-years at risk, 11,884 total deaths. There were 284 cases of death from colon cancer (138 men and 146 women)
- The HRs for colon cancer mortality among men with a high intake of one of several types of meat (beef, pork or chicken) compared with men with a low intake of that meat exceeded 1.0. However, only the comparison with medium and low intakes of chicken was statistically significant (adjusted HR=1.7; 95% CI=1.1-2.6). There was no significant (NS) positive or negative association of meat consumption with rectal cancer in men or with colon or rectal cancer in women
- Yogurt intake was negatively associated with the risk of rectal cancer in men (P=0.04); the risk for the high-intake group was less than one-half the risk for the low-intake group
- In women, there was a significant positive association of cheese intake and rectal cancer mortality (HR for high- vs. low-intake groups=2.5; 95% CI=1.1-5.7)
- Green leafy vegetable were the only vegetables to show a significant negative association with male rectal cancer mortality (P=0.02; 0.57 (95% CI=0.3-0.9)
- In women, there was NS association between vegetable consumption and colorectal cancer mortality
- Fruit intake in women was positively associated with risk of colon cancer (P=0.04)
- Egg consumption was significantly associated with colon cancer mortality only in men (HR for high- vs. low-intake=1.5; 95% CI=1.0-2.4; P=0.04)
- Fish, tofu, boiled rice and mushroom consumption were not related to colorectal cancer risk in men or women
- The following items had power values less than 50% for detection of the RR of 2.0: beef, yogurt, carrot and tomato for male colon cancer; beef, carrot and tomato for male rectal cancer; and beef for female colon cancer. Due to the small number of female rectal cancer, most items (except for milk, egg and tofu) had power values of <50%.

Hazard Ratio[a] and 95% Confidence Interval for Colon and Rectal Cancer Mortality According to Intake Frequency of Yogurt and Green Leafy Vegetables in Men as Well as Fruit and Eggs in Women.

	Colon Cancer					Rectal Cancer			
Food Frequency	**Person-years**	**Number of cases**	**Adjusted HR**	**(95% CI)**	**P for Trend**	**Number of Cases**	**Adjusted HR**	**(95% CI)**	**P for Trend**
Yogurt in men									
Low (seldom)	208,876	52	1.00		0.37	56	1.00		0.04
Middle (one to two per month)	45,889	15	1.32	(0.74-2.35)		9	0.80	(0.39-1.62)	
High (one to seven per week)	50,482	12	0.80	(0.42-1.51)		7	0.46	(0.21-1.02)	
Green leafy vegetables in men									

Low (zero to two per week)	146,277	34	1.00		0.40	46	1.00		0.02
Middle (three to four per week)	102,066	43	1.63	(1.03-2.55)		26	0.74	(0.46-1.20)	
High (every day)	104,077	36	1.19	(0.74-1.91)		23	0.57	(0.34-0.94)	
Fruit									
Low (zero to two per week)	142,584	28	1.00		0.04	12	1.00		0.35
Middle (three to four per week)	117,048	27	1.25	(0.73-2.13)		9	0.91	(0.38-2.19)	
High (every day)	201,190	60	1.62	(1.02-2.57)		10	0.53	(0.22-1.26)	
Eggs									
Low (zero to two per week)	118,645	27	1.00		0.04	37	1.00		0.50
Middle (three to four per week)	117,116	37	1.40	(0.84-2.31)		21	0.56	(0.33-0.96)	
High (every day)	188,707	70	1.54	(0.99-2.42)		52	0.82	(0.54-1.26)	

[a]Adjusted HR: hazard ratio adjusted for age, family history of colorectal cancer, BMI, frequency of alcohol intake, current smoking status, walking time per day and educational level and stratified by regions by Cox proportional hazard model.

CI: confidence interval estimates.

Author Conclusion:

Due to small sample size and the measurement error in the study, the authors were unable to draw firm conclusions about the relationship between colorectal cancer and diet in Japan.

Reviewer Comments:

The authors noted the following limitations:

- *The number of identified cases for rectal cancer was low*
- *The population may be too homogenous*
- *The end-point was death due to colon or rectal cancer, the risks reported were for fatal colon and rectal cancer and not for cancers amendable to treatment.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes

7.1.		Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.		Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.		Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.		Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.		Was the measurement of effect at an appropriate level of precision?	Yes
7.6.		Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.		Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
8.1.		Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.		Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.		Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.		Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.		Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.		Was clinical significance as well as statistical significance reported?	Yes
8.7.		If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
9.1.		Is there a discussion of findings?	Yes
9.2.		Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
10.1.		Were sources of funding and investigators' affiliations described?	Yes
10.2.		Was the study free from apparent conflict of interest?	Yes